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"Passive" Exposure of Asthmatic Subjects to Cigarette Smoke

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Fourteen asthmatic subjects volunteered for a controlled trial of 2-hr passive exposure to cigarette smoke. Seven cigarettes were burnt in a closed room of 14.6-m³ capacity, producing a carbon monoxide concentration 24 ppm above ambient and a suspended particulate concentration of 2–4 mg·m⁻³. Most symptomatic responses were as in normal individuals, but there were more complaints of wheezing (36%) and tightness in the chest (43%). Changes of pulmonary function were slight. Relative to the corresponding control exposure, there was a small decrease of total lung capacity as assessed by helium mixing ($P < 0.02$), possibly indicating an effect of the smoke on small airways. There was also some evidence of arousal and or emotional excitement, including a slight tachycardia (at 60-min exposure, $P < 0.05$) and a slight increase of forced vital capacity ($P < 0.05$ at 90-min exposure). However, dynamic lung volumes ($FEV_{1.0}$, V_{max} at 50% V_{max}) were unaltered. Examining separately the four subjects who claimed sensitivity to cigarette smoke, the only significant difference from the remaining asthmatic individuals was a greater $FEV_{1.0}$ relative to the corresponding time in the control exposure. Our data thus do not support that asthmatic subjects have an unusual sensitivity to cigarette smoke.

INTRODUCTION

There is now good documentation concerning the accumulation of particulate matter, irritant gases, and vapors that results from the smoking of cigarettes in a closed and poorly ventilated space (see Sebben *et al.*, 1977; Pimm *et al.*, 1978; Shephard *et al.*, 1978). Nevertheless, physiological responses to such pollutants are remarkably slight in normal adults. The breakup of the tear film is significantly accelerated (Basu *et al.*, 1978), but both acute (Pimm *et al.*, 1978; Shephard *et al.*, 1979a) and chronic (Schilling *et al.*, 1977) changes of airway resistance are usually small and statistically insignificant even when high concentrations of smoke have been used and subjects have been required to perform intermittent exercise during exposure (Shephard *et al.*, 1979a).

Argument continues over the existence of respiratory allergies to tobacco smoke (Speer, 1968; Zussman, 1970; Blue, 1970; Savel, 1970). Although formal immune responses have yet to be demonstrated, wheezing following "passive" exposure to cigarettes is more than twice as frequent in asthmatics as in non-asthmatics (Shephard *et al.*, 1979b). It was thus thought of interest to make an assessment of symptoms and objective airway responses in a group of asthmatic adults passively exposed to controlled concentrations of cigarette smoke.

METHODS

Subjects and experimental plan. The subjects were 14 volunteers attending the Asthma Clinic of The Gage Research Institute. Physical characteristics and baseline lung function data are given in Table 1. The diagnosis was reached ac-

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TABLE 1

PHYSICAL CHARACTERISTICS OF SUBJECTS (MEAN ± SD, RANGE) AND BASELINE PULMONARY FUNCTION DATA (PERCENTAGE PREDICTED* ± SD)

Physical characteristic	Men (n = 9)	Women (n = 5)	All subjects (n = 14)
Age (years)	44 ± 14 (27–65)	33 ± 8 (19–38)	
Height (cm)	173.6 ± 10.0 (161–194)	163.6 ± 8.6 (157–178)	
Weight (kg)	73.7 ± 10.3 (54.3–86.1)	62.3 ± 7.7 (56.5–75.3)	
FVC	98 ± 19 (57–128)	107 ± 12 (91–123)	101 ± 17 (57–128)
$FEV_{1.0}$	68 ± 19 (30–91)	84 ± 23 (60–113)	74 ± 21 (30–113)
$\dot{V}_{max\ 50\%VC}$	44 ± 23 (16–81)	66 ± 39 (21–106)	52 ± 30 (16–106)
FRC	90 ± 11 (76–104)	100 ± 18 (85–125)	94 ± 14 (76–125)
RV	93 ± 27 (63–152)	98 ± 27 (67–136)	95 ± 26 (63–152)
TLC	99 ± 10 (87–118)	102 ± 10 (94–119)	100 ± 10 (87–119)

* Based on norms adopted for Toronto laboratories by Toronto Interhospital Respiratory Disease Committee.

cording to the standard criteria of The Gage Research Institute, namely: (i) a history consistent with diffuse intermittent airway obstruction, and (ii) diffuse expiratory bronchi and/or reversible airway obstruction demonstrated by a >15% increase of $FEV_{1.0}$ or $\dot{V}_{max\ 50\%VC}$ 20 min following inhalation of salbutamol. Associated chronic bronchitis or pulmonary emphysema was not a contraindication to participation but no tests were carried out during acute respiratory infections or exacerbations of the asthma. All subjects continued with their normal medication on experimental days (Table 2). The median methacholine sensitivity (as judged from the concentration needed to induce a 20% fall of $FEV_{1.0}$) was 3.1 mg/ml, and the gain of $\dot{V}_{max\ 50\%VC}$ with four puffs of salbutamol ranged from 10 to 341% (median 30%).

Each subject sat in a small (14.6 m^3) room for 2 hr on two occasions: at one visit, the room contained ambient air, and on the other occasion it was heavily contaminated by cigarette smoke from a smoking machine, the order of the experiments being determined by lot. A battery of lung function tests was performed before, during, and after exposure, and heart rates were also monitored at 10-min intervals. Subjects were questioned as to symptoms they anticipated on entering the chamber, and those they actually encountered on leaving the chamber.

Smoke generation. The cigarette smoking machine was of the type described by

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TABLE 2

NORMAL MEDICATIONS, CONCENTRATION OF METHACHOLINE NEEDED TO INDUCE 20% FALL OF $FEV_{1.0}$, AND CHANGE OF FUNCTIONS INDUCED BY FOUR PUFFS OF VENTOLIN

Subject	Medication						Methacholine sensitivity	Percentage change of function after four puffs of ventolin		
	"Tedral"	"Choledyl"	"Beclomet"	"Alupent"	"Prednisone"	"Ventolin"		FVC	$FEV_{1.0}$	V_{max} 50%
Hr	R	—	—	—	—	P	Not done	Not done	Not done	Not done
Ba	—	R	—	—	—	—	>25 mg/ml	2	8	29
Ch	—	R	R	—	—	P	3.1	22	48	Not done
Co	—	—	—	—	—	O	1.6	Not done	Not done	Not done
Se	—	—	R	—	—	P	12.3	3	22	Not done
Hr	—	—	R	—	R	P	1.6	30	53	99
Fe	—	R	R	—	—	—	1.6	9	48	59
Sc	—	P	R	—	R	P	3.1	10	111	284
Ba	—	P	—	—	P	P	0.8	9	11	10
Mo	—	—	—	—	—	P	Not done	0	10	25
Hi	—	—	R	R	—	—	Not done	2	7	31
La	—	R	R	—	—	P	Not done	9	24	141
Ro	R	—	—	—	—	P	Not done	0	11	28
Mc	—	—	—	—	—	—	<25 mg/ml	−3	1	19

* Dimenedihalerus needed, R = regular, O = occasional, P = as needed. Tedral = theophylline + ephedrine + phenobarbital, prednisone = orciprenaline sulphate, ventolin = salbutamol, choledyl = oxtriphylline, beclomet = beclamethasone, and alupent = delta cortisone.

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Wynder and Hoffman (1967). Prior to exposure, four cigarettes were "smoked" simultaneously, with combustion of one further cigarette at 30-min intervals in order to maintain smoke concentrations. A small peristaltic pump connected to a series capacity vessel drew one brisk (2-sec) but controlled (35-ml) puff through the apparatus, discharging the "mainstream" smoke into the room after passage through the solenoids, capacity vessel, and pump. "Sidestream" smoke escaped directly into the room.

The cigarettes used were a popular 85-mg filter type, with reported values for tar and nicotine content of 19 and 14 mg, respectively; they were smoked to a butt length of about 23 mm. Preliminary experiments established that with the pattern of combustion used, a carbon monoxide concentration of 24 ppm above ambient was developed and sustained. The initial suspended particulate concentration was >4 mg/m³, but values dropped to ~ 2 mg/m³ over the 2-hr exposure period.

Pulmonary function studies. At the beginning and the end of each 2-hr experiment the relaxed vital capacity (RVC), functional residual capacity (FRC), residual volume (RV), and total lung capacity (TLC) were measured by a closed-circuit helium katharometer System (Collins modular lung analyzer).

Flow/volume loops were measured on entering the exposure chamber, and at

TABLE 3

POTENTIAL SYMPTOMS DURING "PASSIVE" CIGARETTE EXPOSURE—NUMBER OF SUBJECTS ANTICIPATING EACH SYMPTOM, AND REPORTED SEVERITY ON SIX-POINT SCALE WHEN COMPLETING A QUESTIONNAIRE AT THE END OF EXPOSURE

Symptom	Number anticipating symptom (n = 13)*	Severity (n = 14)					
		Absent (= 0)	Trace (= 1)	Mild (= 2)	Moderate (= 3)	Severe (= 4)	Incapacitating (= 5)
Nasal discharge or stuffiness	6	10	0	4	0	0	0
Shortness of breath	3	11	0	2	1	0	0
Wheezing	4	9	1	2	2	0	0
Tightness in chest	3	8	5	1	0	0	0
Cough	6	9	2	3	0	0	0
Sputum	1	11	1	2	0	0	0
Sore throat	2	12	0	2	0	0	0
Eye irritation	4	1	1	9	3	0	0
Nausea	1	14	0	0	0	0	0
Dizziness	2	14	0	0	0	0	0
Headache	1	11	0	3	0	0	0
Fatigue	0	11	0	3	0	0	0

* No data for one subject.

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30-min intervals thereafter. Flow and volume signals were obtained from a Fleisch (No. 3) pneumotachograph and integrator, the corresponding loops being displayed on a Tectronix storage oscilloscope. At each test, the subject was seated and performed three maximum forced vital capacity (FVC) maneuvers. The loop with the largest FVC was analyzed for measurements including FVC, the 1-sec forced expiratory volume ($FEV_{1.0}$), and maximum flow rates at 25% ($\dot{V}_{max\ 25\%}$) and 50% ($\dot{V}_{max\ 50\%}$) of vital capacity.

Heart rates. The electrocardiogram was monitored by a Sanborn 500 Visicardiette recorder throughout exposure, using chest leads fixed in the CM_5 position. Recordings were made at 10, 20, 40, 50, 70, 80, 100, and 110 min for the purpose of counting heart rates.

Symptoms. Subjects were asked to describe the symptoms they anticipated prior to entering the smoke-filled chamber. At the end of exposure, they were handed a list of 12 possible symptoms, and were required to rate each on a 6-point scale, ranging from absent (0) through trace (1), mild (2), moderate (3), severe (4), and incapacitating (5).

RESULTS

Symptoms

The number of symptoms reported on the questionnaire were somewhat greater than the reactions anticipated by the subjects prior to exposure (Table 3). The biggest discrepancy was for eye irritation, marked as present by all except one subject on the final questionnaire, but anticipated by only 4 of 13 subjects.

The commonest anticipated complaints were cough and nasal discharge or stuffiness. Shortness of breath, wheezing, or tightness in the chest were expected by only five of the group.

Static Lung Volumes

Initial values for static lung volumes were on average close to normal predicted results (Table 1). At the end of the 2-hr sham exposure, RV and TLC tended to

TABLE 4

EFFECTS OF SITTING IN EXPOSURE CHAMBER (SHAM EXPOSURE) AND "PASSIVE" EXPOSURE TO CHAMBER SMOKE UPON STATIC LUNG VOLUMES*

Variable	C_{2h}/C_0 (%)	E_2/C_0 (%)	E_{2h}/C_{2h} (%)
Relaxed vital capacity	99.8 ± 6.8	99.8 ± 5.3	98.0 ± 5.3
Residual volume	107.4 ± 19.2	109.6 ± 19.4	93.0 ± 16.4
Functional residual capacity	101.8 ± 9.3	103.9 ± 7.9	95.2 ± 13.1
Total lung capacity	102.8 ± 5.5	103.5 ± 3.4 **	96.5 ± 4.6**

* Data expressed as percentage of sham exposure at zero time (C_0) or at end of sham exposure (C_{2h}).
Mean ± SD.
$P < 0.1$.
$P < 0.02$.
$P < 0.01$.

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TABLE 5

EFFECTS OF SETTING IN EXPOSURE CHAMBER (SHAM EXPOSURE) AND "PASSIVE" EXPOSURE TO CIGARETTE SMOKE UPON DYNAMIC LUNG VOLUMES*

Variable	C_{1m}-C_0 (%)	E_m-C_0 (%)	E_m-C_m (%)	E_{nm}-C_{nm} (%)	E_{1m}-C_{1m} (%)	E_{1m}-C_{1m} (%)
FVC	102.1 ± 5.4	101.3 ± 2.9	101.0 ± 7.4	100.1 ± 4.7	103.9 ± 6.5	100.6 ± 5.0
$FEV_{1.0}$	105.9 ± 14.4	103.1 ± 11.6	102.1 ± 11.5	99.2 ± 12.1	102.1 ± 9.9	101.4 ± 7.9
$\dot{V}_{max\ 75}$	156.1 ± 121.0	101.6 ± 45.3	92.4 ± 45.6	86.6 ± 33.4	119.5 ± 56.0	124.8 ± 85.0
$\dot{V}_{max\ 50}$	114.4 ± 37.6	97.6 ± 27.8	96.4 ± 22.8	94.1 ± 17.3	102.9 ± 27.0	99.6 ± 26.9

* Data expressed as percentage of sham exposure at zero time (C_0) or at corresponding time in sham exposure (C_m, C_{nm}, C_{1m}). Mean ± SD.
* $P < 0.1$.
** $P < 0.05$.

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increase, but not significantly so (Table 4). The FRC and TLC on the experimental day were larger than those measured prior to the sham exposure, the difference being particularly significant ($P < 0.01$) for the TLC. These discrepancies were reversed over the 2-hr passive exposure to cigarette smoke, and at the end of the experiment the TLC was less than on the sham exposure day ($P < 0.02$).

Dynamic Lung Volumes

The initial FVC was close to predicted normal values, but as would be anticipated there was a substantial impairment of $FEV_{1.0}$ and $\dot{V}_{max\ 50\%VC}$ (Table 1). Two hours of sham exposure tended to increase late expiratory flow rates, the trend being of marginal significance ($P < 0.1$) for $\dot{V}_{max\ 50\%VC}$ and $\dot{V}_{max\ 25\%VC}$ (Table 5). There was remarkably little change of dynamic volumes during passive cigarette smoke exposure relative to the corresponding sham exposure, the one statistically significant finding ($P < 0.05$) being a small increase of FVC at 90 min of exposure.

Heart Rates

Heart rates did not change significantly over the 2-hr sham exposure. [redacted] 05) in the 80th min of exposure.

Subjects Claiming Cigarette Smoke Sensitivity

Data were analyzed separately for the four subjects who anticipated the symptom of wheezing during passive cigarette smoke exposure, and the ten who did not anticipate this response. On the experimental day, the "sensitive" subgroup tended to an increase of residual volume, functional capacity, and total lung capacity relative to other subjects (Table 7). However, they showed a similar difference of behavior during the sham exposure, so that when each individual's sham exposure was used as the control data ($E_{120}/C_{120}\%$), residual volume, func-

TABLE 6

EFFECTS OF SITTING IN EXPOSURE CHAMBER (SHAM EXPOSURE) AND "PASSIVE" EXPOSURE TO CIGARETTE SMOKE ON HEART RATE*

Time (min)	Sham exposure percentage C_0 (%)	Passive exposure, percentage of corresponding sham exposure C_t (%)
0	100	102 ± 16
10	97 ± 5	104 ± 11
20	96 ± 7	105 ± 14
40	98 ± 8	102 ± 8
50	98 ± 8	103 ± 10
70	98 ± 8	102 ± 9
80	93 ± 8	106 ± 11
100	96 ± 7	102 ± 15
110	97 ± 9	104 ± 19

* Data expressed as percentage of sham exposure at zero time (C_0) or at corresponding time C_t during sham exposure ($C_{10, 20, 40, 50, 70, 80, 100, 110}$), mean ± SD.

$P < 0.05$.

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TABLE 7

RESPONSES OF SUBJECTS ANTICIPATING WHEEZING ("SENSITIVE" S, $n = 4$) RELATIVE TO REMAINDER OF GROUP (OTHER, 0), (MEANS FOR EACH CATEGORY)[a]

	E_{120}/E_0 (%)		C_{120}/C_0 (%)		E_{120}/C_{120} (%)	
	(S)	(0)	(S)	(0)	(S)	(0)
Relaxed vital capacity	98	98	100	100	101	97
Residual volume	100	91	120	100	85	97
Functional residual capacity	97	94	107	102	92	96
Total lung capacity	99	94	105	102	97	96
FVC	99	102	103	102	100	101
$FEV_{1.0}$	100	106	103	107	107	99
$\dot{V}_{max\ 25\%\ VC}$	127	153	121	170	103	97[b]
$\dot{V}_{max\ 50\%\ VC}$	95	125	104	119	100	99

[a] Comparison of preexposure and 120 min of exposure (E_{120}/E_0, %). Corresponding sham experiment (C_{120}/C_0, %). Comparison of experimental and sham exposure at 120 min (E_{120}/C_{120}, %).

[b] Omitting one subject with very high value (mean for all subjects = 133).

[c] $P < 0.1$.

[d] $P < 0.05$.

[e] $P < 0.01$.

tional residual capacity, and total lung capacity on the experimental day were reduced at least as much in the "sensitive" subjects as in the remainder of the sample.

Taking data for the experimental day, the "sensitive" subgroup tended to a decline of dynamic lung volumes relative to the behavior of the other subjects, the discrepancy approaching significance for the $\dot{V}_{max\ 50\%\ VC}$ (Table 7). Again, there was a tendency for a similar discrepancy between the two subgroups on the sham exposure day, so that when the individual's sham exposure data was used as a control (E_{120}/C_{120}%), all values for "sensitive" and "other" subjects agreed to within 5–6%; the only statistically significant difference was a small increase of $FEV_{1.0}$ in the "sensitive" subjects.

DISCUSSION

Behavior Relative to Nonasthmatic Subjects

The frequency and severity of most symptoms was much as reported for normal subjects exposed to a comparable concentration of cigarette smoke (Pimm *et al.*, 1978; Shephard *et al.*, 1979a) (Table 8), with the exception that almost a half of the asthmatic sample complained of wheezing and tightness in the chest. Coughing was more severe in the normal subjects, although this is probably related to the fact that they performed intermittent exercise and thus received a greater dose of smoke than the asthmatic individuals. The latter were observed while sitting at rest because of the problem that exercise would of itself have provoked bronchospasm in this group.

The physiological changes observed in normal subjects during smoke exposure, although occasionally reaching conventional levels of statistical significance, were of doubtful biological importance (Pimm *et al.*, 1978; Shephard *et al.*, 1979a).

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TABLE II

A Comparison of Symptoms in Normal and in Asthmatic Subjects during "Passive" Exposure to Cigarette Smoke*

Symptom	Percentage affected: Normal subjects: Rest (%)	Percentage affected: Normal subjects: Intense exercise (%)	Percentage affected: Asthmatic subjects: rest (%)	Average symptom score: Normal subjects: Intense exercise	Average symptom score: Asthmatic subjects: rest
Nasal discharge or stuffiness	35	33	28	0.33	0.61
Shortness of breath	15	17	21	0.33	0.30
Wheezing	10	0	36	0.00	0.84
Tightness in chest	5	0	43	0.00	0.46
Cough	45	58	36	1.08	0.54
Sputum	30	8	21	0.08	0.31
Eye irritation	95	92	93	2.67	1.92
Nausea	10	0	0	0.00	0.00
Dizziness	10	25	0	0.42	0.00
Headache	15	25	21	0.58	0.46
Fatigue	0	17	21	0.33	0.46

* Percentage of subjects reporting the symptom, average symptom score based on the reported intensity of a given symptom ranging from 0 = absent to 3 = incapacitating).

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Findings included some increase of heart rate and respiratory minute volume, probably of emotional origin, a tendency of increase in functional residual capacity and residual volume in some experiments, and small decreases of dynamic lung volumes. The asthmatic subjects also showed emotional reactions to the cigarette smoke, including the tachycardia, and possibly the preexposure increase of FRC and TLC. Taking the group as a whole, there was no evidence of impairment of dynamic lung volumes during the passive cigarette exposure. It might be argued that emotional reactions to the smoke-filled chamber were sufficient to mask such a response. However, we did not form the impression that subjects were unduly alarmed by the experiment, and the observed tachycardia after 2-hr passive smoke exposure was slight. We did not measure serum or urinary nicotine levels, but again the absence of any marked tachycardia speaks against a nicotine-mediated release of epinephrine. Russell and Feyerabend (1975) concluded that the rapid excretion of nicotine made a systemic pharmacological action an improbable sequel to sustained passive cigarette smoke exposure. We would thus conclude that there was little likelihood of a sufficient increase in sympatho-adrenal activity, emotional or pharmacological, to counteract cigarette smoke-induced bronchospasm.

The most interesting observation is the small decrease of TLC as measured by helium dilution (Table 4). This could imply an effect of the smoke upon the small airways, with an increase of gas trapping, and it would be worthwhile to extend observations using some more specific measures of small airway function such as helium flow–volume curves.

Sensitive Subjects

Although several of the asthmatic subjects claimed wheezing and tightness in the chest would result from passive exposure to cigarette smoke, the physiological data give little support to the concept of a subgroup with particular sensitivity.

On the experimental day, the group claiming sensitivity showed a tendency of increase in static lung volumes, and a decrease in dynamic volumes. However, changes were of almost equal magnitude during the sham exposure. We may thus hypothesize that the observed reactions are due to the suggestibility of the subjects rather than a pharmacological or allergic reaction to cigarette smoke. In support of this view, the only significant difference in the "sensitive" group was a greater $FEV_{1.0}$ relative to the corresponding time in the control exposure, presumably due to greater sympathetic activation and/or arousal in the smoke-filled environment.

Implications for Air Quality Legislation

While there may be valid grounds for controlling the cigarette smoke concentration in "public" air (Shephard *et al.*, 1979a), the present data offer little support to the view that asthmatic subjects need special consideration in this regard. Complaints of tightness in the chest and wheezing were more frequent than in the general population, but the only statistically significant physiological response was a very small decrease of TLC. Further, this change was not significantly greater in those complaining of chest symptoms. The subjective reactions thus

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seem but one more manifestation of annoyance, almost universal at the concentration evaluated.

[redacted] might have been considered at higher smoke concentrations. Nevertheless, the value used is the highest likely figure to which an asthmatic subject will be exposed (Sebben *et al.*, 1977), and indeed with adequate ventilation smoke concentrations can be held to substantially lower figures.

We would thus conclude that the specific sensitivity of asthmatic subjects is not a major consideration when determining air quality criteria for rooms contaminated by cigarette smoke.

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REFERENCES

Basu, P. K., Pimm, P. E., Shephard, R. J., and Silverman, F. (1978). The effect of cigarette smoke on the human tear film. *Canad. J. Ophthalmol.* 13, 22–26.

Blue, J. A. (1970). Cigarette asthma and tobacco allergy. *Ann. Allergy* 28, 110–115.

Pimm, P., Shephard, R. J., and Silverman, F. (1978). Physiological effects of acute passive exposure to cigarette smoke. *Arch. Environ. Health* 33, 201–203.

Russell, M. A. H., and Feyerabend, C. (1975). Blood and urinary nicotine in non-smokers. *Lancet* I, 179–181.

Savel, H. (1970). Clinical hypersensitivity to cigarette smoke. *Arch. Environ. Health* 21, 146–148.

Schilling, R. S. F., Letai, A. D., Hui, S. L., Beck, G. J., Schoenberg, J. B., and Bouhuys, A. (1977). Lung function, respiratory disease, and smoking in families. *Amer. J. Epidemiol.* 106, 274–283.

Sebben, J., Pimm, P., and Shephard, R. J. (1977). Cigarette smoke in enclosed public facilities. *Arch. Environ. Health* 32, 53–58.

Shephard, R. J., and LaBarre, R. (1978). Attitudes of the public towards cigarette smoke in public places. *Canad. J. Publ. Health* 69, 302–310.

Shephard, R. J., Collins, R., and Silverman, F. (1979a). Responses of exercising subjects to acute "passive" cigarette smoke exposure. *Environ. Res.*, 19, 279–291.

Shephard, R. J., Pemsford, I., LaBarre, R., and Basu, P. K. (1979b). Subjective reactions to passive cigarette-smoke exposure. Effect of cigarette smoke on the eyes and airways. *Int. Arch. Occup. Environ. Health.* 43, 135–144.

Speer, F. (1968). Tobacco and the non-smoker. A study of subjective symptoms. *Arch. Environ. Health* 16, 443–448.

Wynder, E. L., and Hoffman, D. (1967). "Tobacco and Tobacco Smoke. Studies in Experimental Carcinogenesis." Academic Press, New York.

Zussman, B. M. (1970). Tobacco sensitivity in the allergic patient. *Ann. Allergy* 28, 371–377.

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